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10/564,494	06/27/2006	Gary P. Cook	02181.0087U2	9161

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EXAMINER	
SHOMER, ISAAC	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/564,494	COOK, GARY P.	
	Examiner	Art Unit	
	ISAAC SHOMER	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 October 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18,20-33 and 35-50* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,18,20-33 and 35-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *13 October 2009, 5 November 2009*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 13 October 2009, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Election/Restrictions

The examiner rejoins Groups I, III, and IV, as they appear to be directed to identical processes wherein controlled release compositions are prepared.

Claim Objections

Claims 5, 23, and 40 are objected to because of the following informalities: There is a missing comma between lecithin and vitamin E-TGPS.

Claim 27 is objected to because of the following informalities: Claim 27 recites "The process of claim 18 wherein said controlled release composition is selected from the group consisting of microparticles and nanoparticles." Claim 17 depends upon claim 18, which teaches a method of making microparticles. Also see the rejection of claim 27 below under 35 U.S.C. 112 2nd paragraph. For the purposes of examination, the examiner understands the scope of the term "nanoparticles" to be within the scope of the term "microparticles."

Claim Rejections - 35 USC § 112 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 12, 13, 30, 31, 47, and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See, e.g., In re Wilder, 22 USPQ 369, 372-3 (Fed. Cir. 1984). (Holding that a claim was not adequately described because the specification did 'little more than outline goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.')

Mere indistinct terms (such as "synthetic analog" of claims 12, 30, and 47 and "synthetic variation" of claims 13, 31, and 48 used herein), however, may not suffice to meet the written description requirement. This is particularly true when a compound is claimed in purely functional terms. See Univ. of Rochester v. G.D. Searle, 69 USPQ2d 1886 (CAFC 2004) at 1892, stating:

> The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. A description of an anti-inflammatory steroid, i.e., a steroid (a generic structural term) described even in terms of its functioning

> of lessening inflammation of tissues fails to distinguish any steroid from others having the same activity or function. A description of what a material does, rather than of what it is, usually does not suffice.... The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. (Emphasis added).

Conversely, a description of a chemical genus will usually comprise a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus. See Univ. of Calf. V. Eli Lilly, 43 USPQ 2d 1398, 1406 (Fed. Cir. 1997). This is analogous to enablement of a genus under Section 112, ¶ 1, by showing the enablement of a representative number of species within the genus.

A chemical genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. *If the genus has substantial variance, the disclosure must describe a sufficient number of species to reflect the variation within that genus*. See MPEP 2163. The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any *combination of such identifying characteristics that distinguish the claimed invention from other materials* and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient. MPEP 2163.

Here, the specification does not provide a reasonably representative disclosure of useful synthetic analogs and variations generally, a potentially huge genus inclusive of many different compounds having widely divergent structures and functions.

Specifically, the specification discloses only a limited number of species at page 8 line 20 to page 11 line 5 , and these are not viewed as being reasonably representative of the genus in its claimed scope because no readily apparent combination of identifying characteristics is provided, other than the disclosure of those specific species as examples of the claimed genus.

Claim Rejections - 35 USC § 112 2nd Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 8, 24, 26, 27, 35, 41, and 43 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "final concentration" of claims 6, 8, 24, 26, 41, and 43 is indefinite as it is unclear which concentration is final. Where values can vary depending on the basis for their determination, the claimed subject matter may be indefinite. *See* Honeywell Intl. v. Intl. Trade Commn., 341 F.3d 1332, 1340 (Fed. Cir. 2003). (Holding that, where a claimed value varies with its method of measurement and several alternative methods of measurement are available, the value is indefinite when the claim fails to concurrently recite the method of measurement used to obtain it). Accordingly, applicant must specify when the final concentration is calculated (e.g. aqueous phase alone, after the phases are mixed, or after recovery). For the purposes of examination, the examiner

understands the term “final concentration” to read on the final concentration in the aqueous phase prior to the phases being mixed.

Claim 27 recites the limitation "controlled release composition" in claim 18. There is insufficient antecedent basis for this limitation in the claim. Claim 18 recites a microparticle, not a controlled release composition. For the purposes of examination, claim 27 will be examined as if it recites “the process of claim 18, wherein said microparticles are selected from the group consisting of microparticles and nanoparticles,” thereby failing to further limit claim 18.

Claim 35 recites the limitation "an improved process.” This claim is indefinite because it is unclear what the process is being compared with. For the purposes of examination, claim 35 will be examined as if it recites “A process for the production of a microparticle…” wherein the word “improved” is ignored.

Claim Rejections - 35 USC § 102

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 1, 4, 6-12, 14-16, and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Spenlehauer et al. (US Patent 6,120,805).

Spenlehauer et al. (hereafter referred to as Spenlehauer) teaches a method of preparation of microparticles comprising the steps of mixing a copolymer of lactic and

glycolic acid (hereafter referred to as PLGA) with spiramycin (a bioactive agent) in dichloromethane, as of Spenlehauer, column 4 lines 24-38, Example 1. Said solution of PLGA and spiramycin in dichloromethane is subsequently dispersed in an aqueous solution comprising 1% sodium cholate[1], as of Spenlehauer, column 4 lines 24-38, Example 1. Sodium cholate is both an organic anion and a surface active agent (e.g. emulsifier), as of Spenlehauer, (column 2 lines 63-68). The two phases were subsequently homogenized and the organic phase is removed to recover nanoparticles of about 60 nm diameter, as of as of Spenlehauer, column 4 lines 24-38, Example 1.

Claim 1 recites that the organic ion is for reducing the degradation of the bioactive agent. Spenlehauer does not teach using sodium cholate for the purposes of reducing degradation of a bioactive agent. However, the claims are drawn to a method of making a controlled release composition, and claim 1, without the clause "wherein said organic ion is present in the aqueous phase to reduce degradation of said bioactive agent" recites a structurally complete invention. Furthermore, the intended use does not appear to result in a structural difference between the claimed invention and the prior art (the composition taught by Spenlehauer appears to be applicable to making microparticles). Hence, the clause cited above is not considered a claim limitation because it only states the intended result of a method step. See MPEP 2111.04, which noted that "a "whereby clause in a method claim is not given weight when it simply expresses the intended result of a process step positively recited.'"

[1] Sodium cholate has a molecular weight of 430.56, as of sodium cholate MSDS (sciencelab.com), page

Claim Rejections - 35 USC § 103

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claims 2, 3, 5, 18, 20-30, 32, 33, 36-47, 49, and 50 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spenlehauer et al. (US Patent 6,120,805).

Spenlehauer et al. (hereafter referred to as Spenlehauer) teaches a method of preparation of microparticles comprising the steps of mixing a copolymer of lactic and glycolic acid (hereafter referred to as PLGA) with spiramycin (a bioactive agent) in dichloromethane, as of Spenlehauer, column 4 lines 24-38, Example 1. Said solution of PLGA and spiramycin in dichloromethane is subsequently dispersed in an aqueous solution comprising 1% sodium cholate[2], as of Spenlehauer, column 4 lines 24-38, Example 1. Sodium cholate is both an organic anion and a surface active agent (e.g. emulsifier), as of Spenlehauer, (column 2 lines 63-68). The two phases were subsequently homogenized and the organic phase is removed to recover nanoparticles of about 60 nm diameter, as of as of Spenlehauer, column 4 lines 24-38, Example 1. In a separate embodiment, Spenlehauer suggests the use of organic solvents including dichloromethane, toluene, aliphatic alcohols (e.g. ethanol or isopropanol), as well as their mixtures, as of Spenlehauer, column 3 lines 28-38. Also in separate embodiments,

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3 section 9.. Therefore, 1% sodium cholate in water is about 23.2 mM.
[2] Sodium cholate has a molecular weight of 430.56, as of sodium cholate MSDS (sciencelab.com), page 3 section 9.. Therefore, 1% sodium cholate in water is about 23.2 mM.

Spenlehauer teaches the use of the emulsifying agents of albumin (column 4 Example 4 lines 55-61) and lecithin (column 4 Example 6 lines 1-7).

Spenlehauer does not specifically teach that the biodegradable polymer is combined with the organic phase prior to the addition of the bioactive agent, as of claim 18. Spenlehauer further does not teach that the bioactive agent is added to the organic phase prior to the addition of the biodegradable polymer, as of claim 36. However, the change in sequence of adding ingredients does not result in method that is patentably distinct from the method disclosed by the prior art. See MPEP 2144.04(IV)(C).

The specific combination of features claimed (of claims 2, 3, 5, 20, 21, 23, 37, 38, and 40) is disclosed within the broad generic ranges taught by the reference but such "picking and choosing" within several variables does not necessarily give rise to anticipation. Corning Glass Works v. Sumitomo Elec., 868 F.2d 1251, 1262 (Fed. Circ. 1989). Where, as here, the reference does not provide any motivation to select this specific combination of variables, specifically cosolvents of ethyl and isopropyl alcohol and emulsifiers of lecithin and albumin, anticipation cannot be found.

That being said, however, it must be remembered that "[w]hen a patent simply arranges old elements with each performing the same function it had been known to perform and yields no more than one would expect from such an arrangement, the combination is obvious". KSR v. Teleflex, 127 S,Ct. 1727, 1740 (2007) (quoting Sakraida v. A.G. Pro, 425 U.S. 273, 282 (1976)). "[W]hen the question is whether a patent claiming the combination of elements of prior art is obvious", the relevant question is "whether the improvement is more than the predictable use of prior art

elements according to their established functions." (Id.). Addressing the issue of obviousness, the Supreme Court noted that the analysis under 35 USC 103 "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." KSR v. Teleflex, 127 S.Ct. 1727, 1741 (2007). The Court emphasized that "[a] person of ordinary skill is... a person of ordinary creativity, not an automaton." Id. at 1742.

Consistent with this reasoning, it would have obvious to have selected various combinations of various disclosed ingredients specifically cosolvents of ethyl and isopropyl alcohol and emulsifiers of lecithin and albumin, from within a prior art disclosure, to arrive compositions "yielding no more than one would expect from such an arrangement".

Claim 13, 31, and 48 are rejected under 35 U.S.C. 103(a) as being unpatentable over Spenlehauer et al. (US Patent 6,120,805) as applied to claims 1-12, 14-16, 18, 20-30, 32, 33, 36-47, 49, and 50 above, and further in view of Alfven et al. (WO 98/43660 A1).

Spenlehauer et al. (hereafter referred to as Spenlehauer) teaches a method of preparation of microparticles comprising the steps of mixing a copolymer of lactic and glycolic acid (hereafter referred to as PLGA) with a bioactive agent in dichloromethane, followed by dispersing in an aqueous solution comprising 1% sodium cholate, homogenization, and evaporating the organic phase, as of Spenlehauer, column 4 lines

24-38, Example 1, a shown supra. The microparticles prepared by the methods of Spenlehauer are intended for parenteral use, as of Spenlehauer, column 1 lines 23-25. Incorporation of drugs, including vasodilators, is suggested by Spenlehauer, column 2 lines 49-50.

Spenlehauer does not teach the incorporation of oxytocin as the bioactive agent.

Alfven et al. (hereafter referred to as Alfven) teaches the administration of a pharmaceutical composition of oxytocin for the purposes of treating fibromyaglia and navel colic, as of Alfven, page 7 lines 38-39 and page 8 lines 1-9. Administration by parenteral methods, especially intramuscular injection, is suggested by Alfven, page 13 lines 8-16. Oxytocin is effective in lowering blood pressure, as of Alfven, page 7 lines 20-24.

It would have been prima facie obvious for one of ordinary skill in the art to have incorporated oxytocin, as of Alfven, into the microparticles made by the method of Spenlehauer. This is because Alfven suggests parenteral and injectable administration of oxytocin for therapeutic purposes, including lowering of blood pressure. As Spenlehauer suggests the incorporation of various drugs, including vasodilators, one of ordinary skill in the art would have been motivated to have incorporated oxytocin into the method of making microparticles of Spenlehauer.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to ISAAC SHOMER whose telephone number is (571)270-7671. The examiner can normally be reached on 8:00 AM - 5:00 PM Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached on (571)272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/I. S./
Examiner, Art Unit 1612

/Frederick Krass/

Supervisory Patent Examiner, Art Unit 1612